UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/522,753 | 03/10/00 | EVANS R | SALK1510-3 |

| EXAMINER | |
|---|---|
| LOEB, B | |
| ART UNIT | PAPER NUMBER |
| 1636 | 10 |

HM22/1010

STEPHEN E REITER
FOLEY AND LARDNER
402 WEST BROADWAY
23RD FLOOR
SAN DIEGO CA 92101-3510

**DATE MAILED:** 10/10/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trad marks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/522,753 | EVANS ET AL. | |
| | Examiner | Art Unit | |
| | Bronwen M. Loeb | 1636 | |

*-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *26-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

This action is in response to the communications filed 2 August 2001.

Claims 1-37 are pending.

### *Election/Restrictions*

1. Applicant's election with traverse of Group I in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the claims are interrelated and a prior art search of one group would involve a search of the other groups. This is not found persuasive because while different inventions may be interrelated, this certainly does not dictate that the searches of the different inventions are interrelated or coextensive. For instance, one can search a polypeptide and it can be found in the art as a result of its function and in the absence of the polynucleotide sequence encoding it. Similarly, a search for an antibody may well encompass only the polypeptide to which it binds and not the polynucleotide sequence encoding the polypeptide.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 26-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

3. Claims 8-13 and 17 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. There was no art found on the elected species, however, so these claims have been examined.

***Sequence Compliance***

4. The Office has corrected minor errors in the computer readable format of the sequence listing. Specifically, the asterisks in the sequence data (e.g. SEQ ID No. 6) have been removed. Applicant does not need to take any action with respect to this information.

5. SEQ ID No. 3 is listed as a 17 nucleotide sequence on p. 38, lines 16-17, in the paper listing and the CRF, however, on p. 66, line 19 of the specification, it is listed as a sequence of nine amino acids.

6. On p. 66, lines 5, 13, 14, 18, 2 and 25, there are references to amino acids 1698-2063 and 2929-3038 of SEQ ID No. 1, however SEQ ID No. 1 in the paper listing has only 1495 amino acids.

7. Figures 2, 5, 6, 9 and 12 have unidentified sequences in them. It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

***Oath/Declaration***

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

There is no signature for Inventor Chen.

***Drawings***

9. The drawings are objected to because Figures 4, 5A, 6C, 9 and 12C are illegible. Correction is required.

***Specification***

10. The disclosure is objected to because of the following informalities: on page 1, the first sentence of the specification refers to an unidentified case. On page 4, line 31, the GenBank accession number is missing. On page 42, line 10, there is no definition provided for the abbreviation "PML". Figure 5 has three panels which is not clearly reflected in the Brief Description of the Drawings. It would be remedial to amend p. 5, line 11 to read "Figures 3A-3D". On p. 42, line 15, there appears to be an incomplete abbreviation in the parentheses. On p. 50, lines 2 and 18, h-SMRT supposedly corresponds to SEQ ID Nos. 3 and 5; SEQ ID No. 3 however is only 17 nucleotides while SEQ ID No. 5 is 2517 amino acids. Also, it is unclear on p. 50, lines 11-12, why

SEQ ID No. 3 is parenthetically referred to with respect to the over 200 amino acids from SEQ ID No. 7. On p. 49, line 24, the h-SMRT clone is indicated as 3.5 kb while on 52, line 12, it is referred to as 5.3 kb. The specification is also objected to as referring to SEQ ID No. 1 as the "full length" SMRT sequence on pp. 42-49 then labeling it as "s-SMRT", presumably for short-SMRT, having then cloned the true full length sequence (in Example 9, p. 49), which is SEQ ID No. 5. On p. 55, line 19, the abbreviation "EcR" is used without a definition being provided.

Appropriate correction is required.

11. The abstract of the disclosure is objected to because it exceeds 150 words in length. Correction is required. See MPEP § 608.01(b) and 37 CFR§1.72.

***Claim Objections***

12. Claim 1 is objected to because of the following informalities: the abbreviation "SMRT" is not defined at its first use in the claim set. Appropriate correction is required.

13. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The specification teaches that the SMRT co-repressors claimed in claim 1 modulate transcriptional potential. The recitation of this limitation in claim 2 therefore does not further limit claim 1 but rather recites an inherent property of the SMRT co-repressors.

### *Double Patenting*

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-7, 19, 21 and 22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6 and 7 of copending Application No. 08/522,726. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species claimed in claim 6 and 7 of copending Application No. 08/522,726 are members of the genus claimed in the instant application in claims 1-7, 19, 21 and 22. A species renders obvious the genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 112*

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-3, 5, 6, 8, 11 and 19-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 64, Number 244, Pages 71427-71440). Claim 1 is drawn to an isolated nucleic acid encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor, or an isoform or peptide portion thereof. This is a genus claim in terms of all members of the family of silencing mediators of retinoic acid receptor and thyroid hormone receptor, or isoforms or peptide portions thereof. Claim 3 is drawn to an isolated nucleic acid wherein the SMRT co-repressor comprises a repression domain having identity to specific amino acids of N-CoR sequence that are less than a given percentage, depending on which specific amino acids of N-CoR are considered. This is a genus claim in terms of all polynucleotides having sequence identities which are less than that recited in claim 3. The specification mentions the human SMRT sequence, one alternative splicing variant of it, a mouse homolog and an apparent splicing variant of the mouse homolog. Also mentioned is human N-CoR and a Drosophila sequence, named SMRTER. This disclosure is not deemed to be descriptive of the complete

structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the family members based on the teachings in the specification. While both the human and mouse homologs appear to have splicing variants leading to "isoforms", the deleted sequences are extremely different. There is no discussion of what the functional significance is of these splicing variants. Deletion analysis indicates that the C-terminal of the human SMRT, N-CoR and mouse SMRT homolog encodes the domain that interacts with the ligand binding domain of RAR and TR and that the N-terminal domain has the repression activity. There are indications of shared domains within the N and C-terminal domains however there is no disclosure of what specific amino acid residues correllate directly with the co-repression activity of these homologs. Furthermore, the Drosophila SMRTER sequence which interacts with ecdysone receptor in a two-hybrid screen, has regions of significant homology with SMRT and N-CoR but is apparently not considered a homolog of these proteins (see Ex. 19 and Ex. 23). Therefore, the specification does not describe the claimed polynucleotides of the family of SMRT co-repressors in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these polynucleotides at the time of filing the present application. Thus, the written description requirement has not been satisfied.

18. Claims 4, 7, 9, 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 64, Number 244, Pages 71427-71440). Claim 4 is drawn to any polynucleotide that encodes SEQ ID No. 5 or conservative variations thereof. Claim 7 is drawn to any polynucleotide sequence having the sequence of SEQ ID No. 4 or conservative variations thereof. Claim 9 is drawn to any polynucleotide that encodes SEQ ID No. 7 or conservative variations thereof. Claim 12 is drawn to any polynucleotide sequence having the sequence of SEQ ID No. 9 or conservative variations thereof. Each of these are genus claims in terms of any polynucleotide sequence having conservative variations of the recited SEQ ID Nos. The specification mentions SEQ ID No. 4, SEQ ID No. 5, SEQ ID No. 7 and SEQ ID No. 9, each of which has co-repressor activity for RAR and TR. This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the conservative variations based on the teachings in the specification. A very large genus is claimed in each case but only one example is provided in each instance. Therefore, the specification does not describe the claimed polynucleotides in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these polynucleotides at the time of filing the present application. Thus, the written description requirement has not been satisfied.

19. Claims 1-3, 5, 6, 8, 11, 16 and 19-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide

sequence comprising SEQ ID No. 4, 6, 8 or sequence variants or sub-sequences of these or sequences which hybridize to one of these and have co-repression activity for retinoic acid receptor (RAR) and thyroid hormone receptor (TR), does not reasonably provide enablement for any polynucleotides that lack co-repression activity for RAR and TR. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction of guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The present claims are broad. Claim 1 encompasses any polynucleotide that is a member of the family of silencing mediators or isoforms or peptide portions thereof.

The nature of the invention is a family of polypeptides which function as transcriptional co-repressors for RAR and TR.

An analysis of the prior art as of the effective filing date of the present application shows little information is known about transcriptional co-repressors for RAR and TR. There are no prior art teachings of a use for polynucleotide sequences which encode isoforms or peptide portions thereof but lack the co-repression activity for RAR and TR.

The relative skill of those in the art of transcriptional regulation and nuclear hormone receptors is high.

The area of the invention is unpredictable as the means for determining a function and thus perhaps a use for polynucleotide sequences that are isoforms or peptide portions thereof of SMRT co-repressors which lack the co-repression activity for RAR and TR are no better than trial and error.

The present specification provides no teaching of a use for any polynucleotide sequence which encodes that isoforms or peptide portions thereof of SMRT co-repressors but for which the specific co-repression activity for RAR and TR is lacking.

No working examples are disclosed which encompass isoforms or peptide portions of any of the claimed sequences which lack co-repression activity for RAR and TR.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to teach how to use the claimed polynucleotides. One would have to determine a function for each product encoded by each polynucleotide encompassed by the claims. Only if one can determine a function for the product encoded by the polynucleotide can one possibly devise a use for the polynucleotide. Such a task will require extensive trial and error experimentation.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue

experimentation by one of skill in the art to determine how to use all the claimed polynucleotide sequences.

20. Claims 4, 7, 9, 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides that are conservative variations of SEQ ID Nos. 4, 5, 6, 7 and 9 and possess co-repression activity for retinoic acid receptor (RAR) and thyroid hormone receptor (TR), does not reasonably provide enablement for any polynucleotides that are conservative variations of SEQ ID Nos. 4, 5, 6, 7 and 9 and lack co-repression activity for RAR and TR. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction of guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The present claims are broad. Claim 4 encompasses any polynucleotide that encodes SEQ ID No. 5 or conservative variations thereof. Claim 7 encompasses any polynucleotide sequence having the sequence of SEQ ID No. 4 or conservative variations thereof. Claim 9 encompasses any polynucleotide that encodes SEQ ID No.

7 or conservative variations thereof. Claim 12 encompasses any polynucleotide sequence having the sequence of SEQ ID No. 9 or conservative variations thereof.

The nature of the invention is a family of polypeptides which function as transcriptional co-repressors for RAR and TR.

An analysis of the prior art as of the effective filing date of the present application shows little information known about transcriptional co-repressors for RAR and TR. There are no prior art teachings of a use for polynucleotide sequences which are conservative variations of SMRT co-repressors but lack the co-repression activity for RAR and TR.

The relative skill of those in the art of transcriptional regulation and nuclear hormone receptors is high.

The area of the invention is unpredictable as the means for determining a function and thus perhaps a use for polynucleotide sequences that encode conservative variations of SMRT co-repressors which lack the co-repression activity for RAR and TR are no better than trial and error.

The present specification provides no teaching of a use for any polynucleotide sequence which encodes conservative variations of specific sequences but for which the specific co-repression activity for RAR and TR is lacking.

No working examples are disclosed which encompass conservative variations of any of the claimed sequences which lack co-repression activity for RAR and TR.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to

teach how to use the claimed polynucleotides. One would have to determine a function for each product encoded by each polynucleotide encompassed by the claims. Only if one can determine a function for the product encoded by the polynucleotide can one possibly devise a use for the polynucleotide. Such a task will require extensive trial and error experimentation.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to determine how to use all the claimed polynucleotide sequences.

21. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

22. Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite as the phrase "isoform" is not defined in the specification and there is no art-recognized definition of what is considered to be an isoform.

Claim 2 is vague and indefinite as the phrase "modulates transcriptional potential" is not defined in the specification and is not a term of art.

Claims 3, 5 and 15 are vague and indefinite as each recites "hybridizes under stringent conditions" however the specification does not provide any limiting examples of such conditions.

Claims 4, 7, 9 and 12 are vague and indefinite in reciting "conservative variations thereof" as the specification does not define this term and it does not have a specific and discrete art-recognized definition.

Claim 9 is vague and indefinite as being drawn to a polynucleotide but reciting "having an amino acid sequence". A polynucleotide may encode an amino acid sequence but does not have an amino acid sequence.

Claim 10 is vague and indefinite as it recites SEQ ID No. 6 which is a mouse sequence however claim 10 depends on claim 4 which is drawn to a human SMRT co-repressor.

Claim 12 is vague and indefinite as being drawn to a polynucleotide but reciting "having an amino acid sequence". A polynucleotide may encode an amino acid sequence but does not have an amino acid sequence.

Claim 15 is vague and indefinite as it does not recite a verb with respect to the phrase "under stringent conditions" so the metes and bounds of the claim are unclear.

Claim 23 is vague and indefinite as it is unclear whether isolated oligonucleotide cannot hybridize to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031-2517 of SEQ ID No. 5, or if this recitation is an alternative isolated oligonucleotide being claimed.

***Conclusion***

Claims 1-25 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to Dianiece Jacobs, Patent Analyst whose telephone number is (703) 305-3388.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

October 9, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER